

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 285/03306	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/IL 02/01037	International filing date (day/month/year) 25.12.2002	Priority date (day/month/year) 25.12.2002
International Patent Classification (IPC) or both national classification and IPC G01N21/55		
Applicant PROTEOPTICS LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☒ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 22.07.2004	Date of completion of this report 24.03.2005
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**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/L 02/01037**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

Description, Pages

1-25 as originally filed

Claims, Numbers

1-44 filed with telefax on 22.07.2004

Drawings, Sheets

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-13, 40-44 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-13, 40-44
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13, 40-44
Industrial applicability (IA)	Yes: Claims	1-13, 40-44
	No: Claims	

2. Citations and explanations

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see separate sheet

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Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents (D) are referred to in this report:

D1: US-B1-6268125
D2: US-A-6008893
D3: US-A-5313264 (cited by the applicant)
D4: WO-A-02063349
D6: US-A-5917607

2. The common concept of Claims 1, 14 and 27 is the following:

An SPR sensor comprising:
a thin conducting layer...; an illumination system...; and a photosensitive surface...
(see e.g. wording of Claim 1);
as well as a flow cell...(see e.g. wording of Claim 14).

Such an SPR sensor is however known from e.g. D1 (see e.g. col.2, l.62 to col.3, l.7; col.4, 38-67; Figs.1-3) or from D3 (see citation in the Search Report).

Thus, the common concept is not new and not inventive.

The requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the following groups of dependent claims (see also Search Report):

A: Claims 1-13,
B: Claims 14-16, and
C: Claims 27-39

It should be noted that dependent Claims 40-44 are common to each of the three inventions.

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3. The applicant paid three search fees and, consequently, a Search Report for the three inventions was provided.
However, the applicant did not indicate which of the inventions should be examined and/or did not pay the fees for the further inventions to be examined as requested (see "Invitation to restrict or to pay additional fees").
Thus, the first invention was be examined only.

INVENTION A (Claims 1-13 and 40-44):

4. In D1 (see e.g. col.2, l.62 to col.3, l.7; col.4, 38-67; Figs.1-3) an SPR sensor is described comprising nearly all features corresponding to Claim 1.

Claim 1 differs therefrom in the following features:

- A: "At least a portion" of the wall of the flow channel "is formed from an elastic material";
B: "At least one hollow needle..." is arranged; and
C: "A portion" of the wall of the flow channel "is formed by a region of the conducting layer".

However, the use of such hollow needles is well-known in this field; see e.g. D2, col.4, l.25 to col.5, l.41.

To further provide an elastic material at the flow channel in order to inject fluid through this material with the needle is a normal working option.

Finally, the arrangement of the flow cell according to feature C is regarded to be merely one of several straightforward possibilities from which the skilled person would select (see e.g. D1, col.3, ll. 5 and 6), in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.

In view of the paragraphs above, the skilled person would regard it a normal design procedure to combine all the features set out in Claim 1. Thus, the subject-matter of Claim does not involve an inventive step and does not satisfy the criterion set forth in Articles 52(1) and 56 EPC.

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5. In Claims 2-13 and 40-44 only slight constructional changes in the apparatus of Claim 1 are defined which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, these dependent claims do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.
6. If, in spite of the above-mentioned objections, the applicant wishes to proceed further in the regional phase, the following additional points should be noted, i.e. the corresponding amendments provided:
 - 6.1 Also documents D1, D2, D4 and D6 should be mentioned and their contents briefly commented on in the introductory part of the description.
 - 6.2 The introductory part of the description should contain statements agreeing with any independent claim submitted.
 - 6.3 Any new independent claim should be submitted in the two-part form set out in Rule 6.3 (b) PCT.
 - 6.4 In the new set of claims reference signs should be inserted in brackets following those features which are so numbered in the figures (Rule 6.2 (b) PCT).
 - 6.5 If new features are taken into the claims, Article 19 (2) of the PCT should not be infringed and it would probably accelerate the examining process if it were indicated from which part of the application any such features are taken.

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CLAIMS

1. An SPR sensor comprising:
 - a thin conducting layer comprising at least one conductive element formed on a
 - 5 surface of a transparent substrate;
 - an illumination system controllable to illuminate an interface between the conducting layer and the substrate;
 - a photosensitive surface that generates signals responsive to light from the light source that is reflected from a region of the interface;
 - 10 a flow cell formed with at least one flow channel having a lumen defined by a wall at least a portion of which is formed from an elastic material and a portion of which is formed by a region of the conducting layer; and
 - at least one hollow needle having an exit orifice communicating with the needle's lumen and wherein fluid flow is enabled between the flow channel and the needle's lumen by
 - 15 puncturing the elastic material with the at least one needle so that the exit orifice communicates with the flow channel lumen.
2. An SPR sensor according to claim 1 wherein the flow cell is produced from of an elastic material.
- 20 3. An SPR sensor according to claim 1 wherein the flow cell is formed from a relatively non-elastic material having an insert formed from an elastic material and wherein material of the insert forms at least a portion of the wall of the at least one flow channel.
- 25 4. An SPR sensor according to any of claims 1-3 wherein the end of the needle is closed and the exit orifice is located along the length of the needle.
5. An SPR sensor according to any of claims 1-4 wherein when the needle protrudes into the channel it at least partially blocks flow of a fluid from a portion of the channel upstream
- 30 of the needle to a portion of the needle downstream of the needle.
6. An SPR sensor according to claim 5 wherein when the needle protrudes into the channel, the needle blocks substantially all fluid flow from the upstream portion to the downstream portion of the channel.

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7. An SPR sensor according to any of claims 1-6 wherein the needle is formed with a depression in the needle wall and wherein when the needle protrudes into the channel the depression forms a shunt channel between the upstream portion of the channel and another channel and at least a portion of a liquid flowing from the upstream portion of the channel towards the downstream portion is shunted through the shunt channel to the other channel.
8. An SPR sensor according to any of claims 1-7 wherein upon extraction of the needle a sufficient distance from the elastic material a hole made in the elastic material as a result of the puncturing seals.
9. An SPR sensor according to any of claims 1-8 wherein the at least one needle comprises at least two needles for a channel of the at least one channel and to cause a fluid to flow in the channel both needles puncture the elastic material and are positioned to protrude into the channel with their respective orifices communicating with the channel lumen so that fluid may be pumped into the channel via one of the needles and aspirated from the channel via the other of the needles.
10. An SPR sensor according to claim 9 wherein the channel is a blind channel having neither an inlet or outlet orifice.
11. An SPR sensor according to any of claims 1-10 and comprising a fluid pump coupled to the at least one needle controllable to pump fluid into the needle and thereby, when the needle orifice communicates with the flow channel lumen, into the flow channel.
12. An SPR sensor according to any of claims 1-11 and comprising a fluid pump coupled to the at least one needle controllable to aspirate fluid from the needle and thereby, when the needle orifice communicates with the flow channel, from the flow channel.
13. An SPR sensor according to any of claims 1-12 wherein the illumination system comprises:
- an array of light sources;
 - a collimator that directs light from each light source in a collimated beam of light that enters the substrate and is incident on a region of the interface between the substrate and

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conducting layer region that forms the wall portion of each of the at least one flow channel;
and

a light source controller controllable to turn off and turn on a light source in the array independent of the other light sources in the array.

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14. An SPR sensor comprising:

a thin conducting layer comprising at least one conductive element formed on a surface of a transparent substrate;

10 a flow cell formed with at least one flow channel having a lumen defined by a wall a portion of which is formed by a region the conducting layer;

a photosensitive surface that generates signals responsive to light reflected from a region of the interface between the region of the conducting layer that forms the wall portion of each of the at least one flow channel and the substrate; and

an illumination system comprising:

15 an array of light sources;

a collimator that directs light from each light source in a collimated beam of substantially parallel light rays that enters the substrate and is incident on a region of the interface between the substrate and conducting layer region that forms the wall portion of each of the at least one flow channel; and

20 a light source controller controllable to turn off and turn on a light source in the array independent of the other light sources in the array.

15. An SPR sensor according to claim 13 or claim 14 wherein the array is a linear array having an array axis.

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16. An SPR sensor according to claim 15 wherein the axis of the array and a normal to the interface are substantially coplanar.

17. An SPR sensor according to claim 15 wherein the axis of the array and the normal are
30 substantially perpendicular.

18. An SPR sensor according to claim 14 wherein the array is a two dimensional array.

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19. An SPR sensor according to claim 18 wherein the array comprises rows and columns of light sources.
20. An SPR sensor according to claim 19 wherein each column is substantially coplanar with a normal to the interface.
21. An SPR sensor according to claim 19 or claim 20 wherein each row is substantially perpendicular to the normal.
22. An SPR sensor according to any of claims 19-21 wherein light sources in a same column provide light at substantially same wavelengths.
23. An SPR sensor according to any of claims 18-22 wherein all the light sources in the array provide light at substantially same wavelengths.
24. An SPR sensor according to any of claims 19-23 wherein light sources in a same row provide light at different wavelengths.
25. An SPR sensor according to any of claims 14-24 and comprising an optical element having two parallel surfaces through which light from each light sources passes before it is incident on the interface and wherein the optical element is rotatable about an axis perpendicular to the normal so as to change an angle at which light from a given light source is incident on the interface.
26. An SPR sensor according to any of claims 1-25 wherein the at least one conductive element comprises a plurality of conductive elements.
27. An SPR sensor comprising:
a thin conducting layer comprising a plurality of conducting elements formed on a surface of a transparent substrate;
an illumination system controllable to illuminate an interface between the conducting layer and the substrate;
a photosensitive surface that generates signals responsive to light from the light source that is reflected from a region of the interface; and

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a flow cell formed with at least one flow channel having a lumen defined by a wall, portions of which are formed by regions of at least two of the conducting elements.

- 5 28. An SPR sensor according to claim 26 or claim 27 wherein each conductive element is connected to a power source controllable to electrify the conducting element with respect to a reference electrode.
- 10 29. An SPR sensor according to claim 28 wherein the plurality of conductive elements comprises a plurality of conducting strips.
30. An SPR sensor according to claim 29 wherein each of the at least one flow channel crosses over each conducting strip.
- 15 31. An SPR sensor according to claim 28 wherein the plurality of conductive elements comprises a plurality of conducting pixels.
32. An SPR sensor according to claim 31 wherein each of the at least one flow channel passes over at least one conducting pixel and each pixel lies under a flow channel.
- 20 33. An SPR sensor according to any of claims 28-32 and comprising an exclusive reference electrode for each conducting element relative to which the conducting element is electrified.
- 25 34. An SPR sensor according to any of claims 28-32 wherein all the conducting element are electrified relative to a same reference electrode.
35. An SPR sensor according to claim 33 or claim 34 wherein the reference electrode is located on an external surface of the flow cell.
- 30 36. An SPR sensor according to claim 33 or claim 34 wherein the reference electrode is located inside the material from which the flow cell is formed.
37. An SPR sensor according to claim 33 or claim 34 wherein the reference electrode is located on the surface of the substrate.

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38. An SPR sensor according to claim 37 wherein the reference electrode is comb shaped having parallel conducting teeth connected to a common backbone.
- 5 39. An SPR sensor according to claim 38 wherein the conductive elements are located between the conducting teeth.
40. An SPR sensor according to any of claims 1-39 wherein the at least one flow channel has a cross section area less than or equal to about a square millimeter.
- 10 41. An SPR sensor according to any of claims 1-39 wherein the at least one flow channel has a cross section area less than or equal to about 0.5 square millimeters.
42. An SPR sensor according to any of claims 1-39 wherein the at least one flow channel has a cross section area less than or equal to about 0.2 square millimeters.
- 15 43. An SPR sensor according to any of claims 1-39 wherein the at least one flow channel has a cross section area less than or equal to about 0.1 square millimeters.
- 20 44. An SPR sensor according to any of claims 1-43 wherein the at least one flow channel comprises a plurality of channels.